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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,097	04/13/2004	Cynthia C. Bamdad	M1015.70013US01	3158

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EXAMINER
DO, PENSEE T

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,097	BAMDAD ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *485,487-502 and 504* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *485, 487-502, 504* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

This application, 10823097, with PG Pub No. 20050112607 , filed 04/13/2004 and having 1 RCE-type filing therein. This application is a continuation in part of 09631818, filed 08/03/2000 ,now abandoned. Application 09631818 is a continuation in part of 09602689, filed 06/23/2000, now abandoned. Application 09602689 is a continuation in part of PCT/US00/01997, filed 01/25/2000. Application PCT/US00/01997 Claims Priority from Provisional Application 60117126, filed 01/25/1999. Application PCT/US00/01997 Claims Priority from Provisional Application 60132288, filed 05/03/1999. Application PCT/US00/01997 Claims Priority from Provisional Application 60155937, filed 09/24/1999. Application 09631818 is a continuation in part of 09602778, filed 06/23/2000 ,now abandoned. Application 09602778 is a continuation in part of PCT/US00/01504, filed 01/21/2000. Application PCT/US00/01504 Claims Priority from Provisional Application 60116975, filed 01/23/1999. Application PCT/US00/01504 Claims Priority from Provisional Application 60132289, filed 05/03/1999. Application PCT/US00/01504 Claims Priority from Provisional Application 60133148, filed 05/07/1999. Application PCT/US00/01504 Claims Priority from Provisional Application 60133772, filed 05/12/1999.

Claimed Invention

485. (Currently amended) A method for immobilizing colloid particles comprising: allowing a first colloid particle to become immobilized with respect to a second colloid particle by binding interaction between a first chemical or biological species fastened to

the first colloid particle and a second chemical or biological species fastened to the second colloid particle; and determining the immobilization of the first colloid particle with respect to the second colloid particle, wherein at least one of the first or second colloid particle is coated with a self-assembled monolayer (SAM), wherein at least one of the first chemical or biological species or second chemical or biological species is fastened to the first or second colloid particle, respectively, via at least one of a carboxylate group, EDC/NHS chemistry, a nucleic acid sequence, or affinity tag interaction.

Amendment Entry & Claims Status

The amendment filed on January 16, 2009 has been acknowledged and entered.

Claims 485, 487-502, 504 are pending and being examined.

Claims 486 has just been cancelled in this amendment. The limitation of claim 486 has been incorporated into claim 485 in this amendment.

Withdrawn Rejection(s)

Rejections under 103 for claim 485 by Liberti in view of Sigal, and by Masson in view of Sigal in the previous office action are now withdrawn since Applicants have incorporated the limitation of claim 486 into claim 485.

Rejection under 103 for claim 487 is also withdrawn herein because Mirkin fails to teach the first chemical/biological species or second chemical/biological species is fastened to the first or second colloid particle via affinity tag interaction.

Maintained Rejection(s)

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 485, 487-502, 504 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 485 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the signaling entity bound to one of the colloid particles/beads. The specification of the present invention requires a signaling entity bound to either colloid particles/beads (see pg. 27, lines 15-20).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 485, 489-502 and 504 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US 6,984,491) in view of Sigal (US 6,319,670).

Mirkin teaches a method of immobilizing colloid particles comprising allowing a first nanoparticle (colloid) conjugated to first oligonucleotides and a second nanoparticle (colloid) conjugated to second oligonucleotides to bind to each other via the binding of first and second oligonucleotides (see col. 4, line 65-col. 5, line 18). Mirkin also teaches that the gold particles can be functionalized with carboxylic acids (carboxylate group) (see col. 38 line 64). With respect to claim 489, the oligonucleotides interaction is a biological interaction. With respect to claim 492, oligonucleotides are synthetic molecules. (example 17). With respect to claim 493, the nanoparticles are gold colloid particles. (see col. 71, line 34). With respect to claims 494 and 495, Mirkin teaches that the oligonucleotides on either nanoparticles are labeled with an energy acceptor or donor which are fluorescent molecules (equivalent to emissive or absorptive species of the claimed invention). (see col. 7, line 30). With respect to claims 496, 498, 500, and 504, Mirkin teaches that the first oligonucleotides have a sequence complement to a first portion of the sequence of a target nucleic acid, and the second oligonucleotides have a sequence complement to a second portion of the sequence of the target nucleic acid. The nucleic acid is contacted with the two types of nanoparticles having first and second oligonucleotides under conditions for hybridization of the oligonucleotides with the nucleic acid. (common entity-biological material) (see col. 4, line 65-col. 5, line 18). The nucleic acid forms an aggregate of the two nanoparticles. Thus, it is an aggregate forming species. With respect to claim 497, Mirkin teaches the two binding species bind to a common entity which is a colloid particle in figure 13B, the aggregate of nanoparticles. With respect to claims 499 and 501, Mirkin teaches the analyte is a drug

(see col. 27, lines 10-12). With respect to claim 502, Mirkin teaches that the analyte can be an enzyme. (see col. 27, lines 40-42).

However, Mirkin fails to teach a self-assembled monolayer and that the first and second species are protein and that the binding interaction is between a protein and a nucleic acid.

Sigal et al. teaches on col. 7, lines 62-68 that assay ligands can be adsorbed onto surfaces by modification of the ligands with moieties that are known to strongly adsorb on the surface, for example thiols will facilitate adsorption of gold. Alternatively, the assay-ligand may be immobilized by adsorption and/or covalent attachment to a "binding layer" coated on the surface of the particle. For example, an assay-ligand may be covalently attached to an oxide surface (e.g., silica or tin oxide) by attachment to functional groups introduced on the surface of the particle (these functional groups may be introduced by methods well-known in the art, e.g., by coating the particle with a self-assembled layer of a functionalized monomer such as a silane. Similarly, an assay-ligand may be covalently attached to the gold surface of a gold particle by coating the particle by reaction with a functionalized thiol (e.g., to form a self-assembled monolayer). (see col. 8, lines 8-20).

Since it is well known in the art, as taught by Sigal, that a self-assembled monolayer such as thiols layer on gold particles is a layer of moieties that are known to strongly adsorb ligands to the surface of the gold particles, it would have been obvious to one of ordinary skills in the art to coat the gold particles of Mirkin with a SAM as taught by Sigal. Self- assembled monolayer is also known as an orderly layer which,

when bound with ligands, provides discrete binding sites on the particles for the target analytes.

Regarding claims 490 and 491, Mirkin has been discussed above for teaching the present invention except that Mirkin discusses on col. 1, lines 55-60, that methods have been reported for making nanoparticles (Quantum dots) water soluble, allowing the immobilization of protein structure on the quantum dot surface. One involves encapsulation of the core-shell structures with a silica layer.

Thus, it would have been obvious to one of ordinary skills in the art to immobilize protein on the nanoparticles and allow the proteins to bind to each other to form aggregate or to bind to a common entity such as a nucleic acid to study protein-protein interaction of a sample in order to diagnose a disease or condition.

Claims 487 and 488 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin in view of Sigal as applied to claim 485 , and further in view of Went (US 6,150,179).

Mirkin and Sigal have been discussed above.

However, Mirkin and Sigal fail to teach that the species fastened to the colloid particle via a metal binding tag.

Went teaches incorporate metal affinity binding tag such as His-tag into proteins so that the proteins can bind to solid phase. (see col. 20, lines 39-40; col. 58, line 49).

It would have been obvious to one of ordinary skills in the art to use the metal binding tag taught by Went as an affinity binding tag to bind the oligonucleotides or

proteins to the nanoparticles because the nanoparticles are metals and thus such tag would bind with high affinity to the nanoparticles since it is a metal binding tag.

Response to Arguments

Applicant's arguments filed January 16, 2009 have been fully considered but they are not persuasive.

With respect to the 112, 2nd paragraph rejection, Applicants argue that one of ordinary skills in the art would be able to detect the immobilization with or without a label using whichever technique may be available.

This is not found persuasive because there is no label attached to the complex and detection technique depends on the label. Thus, without any label, one of ordinary skill in the art would not be able to detect anything.

With respect to the 103 rejection by Mirkin, Applicants argue that Mirkin fails to teach determining the immobilization of the first colloid particle with respect to the second colloid particle because the Mirkin 's construct cannot be used for detecting single interactions between colloid particles, between a first chemical or biological species fastened to the first and second colloid particles as presently claimed.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "detecting single interactions between colloid particles, between a first chemical or

biological species fastened to the first and second colloid particles) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants also argue that Mirkin teaches particles forming aggregates which is not the same as the method of the presently claimed invention.

The present claims contain opening "comprising" language and therefore fail to exclude the particles that bind together to form an aggregates. Mirkin satisfies the requirement of the present invention by teaching the immobilization of the first colloid particle with respect to second colloid particle via the interaction of the biological/chemical species fastened to the colloid particles.

Applicants also argue that Mirkin fails to teach using self-assembled monolayers (SAM) on the surface of the nanoparticles and further submits that Mirkin teaches away from using SAM on the surface of the nanoparticles.

Sigal is relied upon for the teaching of a SAM on the surface of the nanoparticle. Regarding the argument that Mirkin teaches away from using a SAM on the surface of the nanoparticles. This is not persuasive. First of all, Mirkin teaches functionalizing the surface of nanoparticles with a functional group such as a carboxylate group (see col. 38, line 64). Sigal teaches functionalizing the nanoparticles with functional groups and one well-known method of introducing functional groups to the surface of the particles is to coat a self-assembled monolayer of functionalized monomer such as silane or thiol on gold particles (see Sigal col. 8, lines 8-20). Since Mirkin teaches using functional

groups to immobilize the DNA on nanoparticles and Sigal teaching introducing functional groups by coating a self-assembled monolayer of thiols on gold particles, one of ordinary skills in the art would have been motivated to combine the two references.

Regarding the Sigal reference, Applicants argue that Sigal does not teach a self-assembled monolayer on the surface of the nanoparticles.

Applicants' attention is directed to Sigal, col. 8, lines 8-20 for the teaching of self-assembled monolayer of thiols on gold particles or functional groups on the surface of particles.

Applicants' argument (which is same as above) regarding the 103 rejection by Mirkin in view of Sigal and Went has been considered and are moot in view of the discussion above.

Regarding claim 487, Applicants' argument is moot because claim 487 is now rejected along with claim 488 which is previously rejected in the last office action.

Since claim 487 is now rejected by different references, this office action is still non-final.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pensee T. Do/
Examiner, Art Unit 1641

/Mark L. Shibuya/
Supervisory Patent Examiner, Art Unit 1641